

**National PBM Drug Monograph  
Orlistat (Xenical)  
September 2005**

VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel

**Executive Summary:**

Orlistat is approved for the management of obesity, including weight loss and weight management when used in conjunction with a reduced-calorie diet; reduce the risk of weight regain after prior weight loss; indicated for obese patients with an initial body mass index  $\geq 30$  kg/m<sup>2</sup> or  $\geq 27$  kg/m<sup>2</sup> in the presence of other risk factors. The Department of Veterans Affairs National Center for Health Promotion and Disease Prevention has developed and implemented the Managing Overweight/Obesity for Veterans Everywhere (MOVE) program. The intention of MOVE is to address obesity through a multidisciplinary approach incorporating nutrition, exercise, behavior modification and medical management. Pharmacotherapy for obesity is included in MOVE after patients have tried dietary and behavior interventions for 6-months.

Orlistat is taken orally as 120 mg capsules does three times a in the proximity of meals. Its systemic absorption in minimal and it is eliminated in the feces. In the gastrointestinal tract orlistat prevents the breakdown of triglycerides into free fatty acids, thus inducing a caloric deficit by reducing systemic absorption of fat.

Orlistat's efficacy and safety have been subjected to systematic reviews and meta-analysis by the Cochrane group, AHRQ, and NICE. The reviews have found that orlistat resulted in a greater mean difference in weight loss from placebo (orlistat – placebo) ranging between 2 to 5 kg after 6 or 12 months of treatment. The mean difference in the percent of body weight lost also favored orlistat, 2.9%. The differences in the percentage of patients (orlistat – placebo) achieving a  $\geq 5\%$  or  $\geq 10\%$  weight loss were 21% and 12%, respectively. Weight regain varied but patients treated with orlistat regained 7% to 22% less weight than those treated with placebo after 2-years.

Orlistat has also been shown to improve cardiovascular risk factors such as lipid and glycemic profiles and blood pressure. The impact of these improvements on cardiovascular and other clinical outcomes and mortality is unknown.

The most frequently reported adverse events with orlistat are gastrointestinal and include fatty/oily stools, oily spotting, fecal urgencies and incontinence, and abdominal pain/bloating/dyspepsia. Orlistat can decrease the absorption of fat soluble vitamins and it is recommended that patients take a multivitamin.

The annual cost of orlistat to the VA is \$876. One cost-effective analysis determined that 5 patients need to be treated in order for 1 patient to lose 5% of his/her body weight after 1 year at a cost of \$3421.

It is recommended that orlistat remain non-formulary at VANF level, and that patients currently prescribed orlistat be grandfathered. Nationally, orlistat is to be available to patients meeting criteria-for-use whose prescription was written by a prescriber in the MOVE program (or similar multidisciplinary program).

## **Introduction<sup>1</sup>**

Obesity is the second most preventable cause of death in the United States affecting 31% of adults between the ages of 20 to 70 years. Obesity is a risk factor for hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, stroke, musculoskeletal disorders, and sleep apnea. The total cost of obesity in 1995 was estimated to be \$99 billion.

In 2003, the Department of Veterans Affairs National Center for Health Promotion and Disease Prevention developed the Managing Overweight/Obesity for Veterans Everywhere (MOVE) program. The intention of MOVE is to address obesity through a multidisciplinary approach incorporating nutrition, exercise, behavior modification and medical management. Pharmacotherapy for obesity is included in MOVE after patients have tried dietary and behavior interventions for 6-months.

Sibutramine and orlistat, two FDA-approved prescription weight loss drugs, are not currently on the VA National Formulary and the PBM has been asked to review their formulary status so that they may be more accessible to patients in the MOVE program.

The purposes of this monograph are to (1) evaluate the available evidence of safety, tolerability, efficacy, cost, and other pharmaceutical issues that would be relevant to evaluating orlistat for possible addition to the VA National Formulary; (2) define its role in therapy; and (3) identify parameters for its rational use in the VA.

## **Pharmacology/Pharmacokinetics<sup>2</sup>**

Orlistat is as an irreversible inhibitor of pancreatic and gastric lipases. Inhibition of these enzymes prevents the hydrolysis of dietary fat (in the form of triglycerides) into absorbable free fatty acids. As a result, undigested triglycerides are eliminated in the feces. Thus a caloric deficit is created by reducing the systemic absorption of dietary fat. The therapeutic dose of 120 mg three times a day inhibits dietary fat absorption by approximately 30%.

Orlistat's systemic absorption is minimal and it is not believed to inhibit the activity of other gastrointestinal enzymes.

**Table 1. Orlistat's Pharmacokinetics**

<b>Parameter</b>	<b>Orlistat</b>
Metabolism	Gastrointestinal wall
Elimination	Feces
Half-life	1-2 hours
Protein Binding	>99%
Bioavailability	5% or less

## **FDA Approved Indication(s) and Off-label Uses<sup>2</sup>**

Management of obesity, including weight loss and weight management when used in conjunction with a reduced-calorie diet; reduce the risk of weight regain after prior weight loss; indicated for obese patients with an initial body mass index  $\geq 30 \text{ kg/m}^2$  or  $\geq 27 \text{ kg/m}^2$  in the presence of other risk factors.

## **Current VA National Formulary Alternatives**

There are no agents currently on the VA National Formulary specifically intended for weight loss or maintenance of weight loss.

## **Dosage and Administration<sup>2</sup>**

Orlistat is taken as one 120 mg capsule three times a day either with or within 1 hour of each meal containing fat. The dose should be omitted if the meal is skipped or contains no fat. Patients are to be on a nutritionally balanced, reduced-calorie diet that contains approximately 30% of calories from fat. The daily intake of carbohydrates, protein, and fat should be divided over the three main meals. Patients are

also to take a once daily multivitamin containing fat-soluble vitamins (A, D, E, and K) should be administered at least 2 hours prior to orlistat.

## **Efficacy<sup>3-7</sup>**

### **Efficacy Measures**

#### **Common methodologies used in the clinical trials**

- Inclusion criteria: Body Mass Index (BMI: weight in kg divided by height in m<sup>2</sup>)  $\geq 30$  kg/m<sup>2</sup> or a BMI  $\geq 27$  kg/m<sup>2</sup> with at least one obesity related co-morbidity
- A placebo-controlled run in phase that included dietary interventions.
- Only those patients meeting predetermined criteria were randomized to placebo or sibutramine

#### **Primary outcomes**

- Percent of base line weight lost
- Number of kilograms (kg) lost
- Percent of patients losing 5% or 10% of initial body weight

#### **Secondary Outcomes**

- Change in blood pressure and heart rate
- Change in cholesterol concentration
- Change in BMI
- Change in waist circumference or waist:hip ratio

## **Summary of efficacy findings**

### **Cochrane Review<sup>3</sup>**

An updated systematic review of weight loss/anti-obesity agents by the Cochrane Metabolic and Endocrine Disorders Group published in 2004 included orlistat; only double-blind, placebo-controlled, weight loss or weight maintenance trials were eligible for inclusion.

#### **Weight Loss Trials**

The Cochrane review included 11 orlistat weight loss trials of 1 year duration; 4 of the trials included a second year to evaluate weight maintenance. All 11 studies had similar interventions including orlistat 120 mg three times a day, a 500-600 kcal/day deficit diet, and diet and exercise counseling. Two studies included an orlistat 60 mg three times a day treatment arm, which was found to be ineffective, hence these arms were eliminated from further analysis. Three trials were conducted exclusively in type 2 diabetics, 3 trials included patients with at least one additional cardiovascular risk factor, 3 trials included patients with hypertension (10%-25%) or dyslipidemia (35%-55%), and the remaining 2 trials did not provide a breakdown of their participants. Eight of the 11 studies included a single-blind, placebo run-in phase for 2 to 5 weeks, with 6 of the 8 requiring at least a 75% rate of compliance in order to be randomized; 75% to 93% (mean 86%) enrolled were randomized.

Exclusion criteria included: 1) obesity of endocrine in origin, 2) women of child-bearing potential and not using a reliable form of birth control, pregnant or breast feeding; 3) treatment with a medication which may alter body weight, 4) uncontrolled hypertension 5) previous bariatric surgery, or 6) loss of >3 or 4 pounds in the 3 months prior to screening.

#### *Demographics*

- N = 6021 (range:218 – 892)
- Mean BMI = 35.7 kg/m<sup>2</sup>
- Mean weight = 100 kg
- Mean age = 49 years
- Percent women = 72%
- Percent Caucasian = 80%

## **Table 2. Effect of orlistat minus placebo on primary and secondary outcomes**

Outcome	Number of studies	Difference between orlistat and placebo (95% CI)	Test for heterogeneity(p-value)
<b>Primary Outcomes</b>			
Weight loss, kg			
• Overall	11	2.7 (2.3 – 3.1)	0.22
• Lower risk	5	3.1 (2.4 – 3.7)	0.49
• Higher risk	6	2.5 (2.0 – 3.1)	0.14
Percent weight loss			
• Overall	10	2.9 (2.3 – 3.4)	0.04, I <sup>2</sup> =49%
• Diabetics	4	2.6 (2.1 – 3.0)	0.47
Run-in phase			
• Yes	7	2.6 (1.8 – 3.3)	0.09
• No	4	2.8 (2.4 – 3.3)	0.71
Achieving ≥5% weight loss	11	21.0 (19 – 24)	0.24
Achieving ≥10% weight loss	10	12.0 (8 – 16)	0.001, I <sup>2</sup> =67%
<b>Secondary Outcomes</b>			
Reduction in			
• Total cholesterol, mg/dL	10	-12.9 (-14.7, -10.8)	0.88
• LDL, mg/dL	10	-10.4 (-12.0, -8.5)	0.70
• HDL, mg/dL	8	-0.8 (-7.5, -0.4)	0.33
• TG, mg/dL	7	-4.4 (-15.1, 6.2)	0.02, I <sup>2</sup> =61%
• SBP, mm Hg	9	-1.8 (-2.6, -0.9)	0.52
• DBP, mm Hg	8	-1.6 (-2.4, -0.7)	0.04, I <sup>2</sup> =52%
• Change in HbA1c	4	-0.2 (-0.3, 0.2)	0.4

LDL – low density lipoprotein, HDL – high density lipoprotein, TG – triglycerides, SBP – systolic blood pressure, DBP – diastolic blood pressure, HbA1c – glycosolated hemoglobin. I<sup>2</sup> = amount of variation explained by heterogeneity; values ≥65% indicates substantial heterogeneity.

Change in waist circumference was reported in 5 studies, with the reduction greater in patients taking orlistat compared to placebo; effect size from 0.7 to 3.4 cm (p<0.05) in 4 of the five studies. Due to heterogeneity, the nine trials reporting fasting plasma glucose results could not be pooled. Patients treated with orlistat, compared to placebo, showed greater reductions in fasting blood plasma glucose concentrations ranging from 1.8 to 23.4 mg/dL. The results were statistically significant in five of these studies. Four studies reported changes in glycosolated hemoglobin concentrations, pooled results found a 0.2% (95% CI 0.2% - 0.3%; test for heterogeneity 0.4) greater reduction in patients treated with orlistat compared to placebo.

#### Weight Maintenance Trials

Four orlistat weight loss trials included a continuation phase to assess weight maintenance. A total of 1159 patients entered these continuation phases. All four studies included an orlistat 120 mg three times a day treatment arm (3 of the 4 studies included 60 mg three times day treatment arms). In two studies patients were re-randomized to placebo or orlistat, patients in the other 2 studies continued on their previously assigned treatment. Diets either remained unaltered or were increased by 200-300 kcal/day for those continuing to lose weight.

In all four studies, weight regain during the maintenance phase was similar for the orlistat and placebo groups and the weight differential observed after the weight loss phase was preserved. Patients taking orlistat regained from 0.5% less to 0.5% more weight than those taking placebo. The absolute amount of weight lost during the year was greater in all orlistat treatment arms, thus when weight regain is expressed as a percentage of weight lost during year one, orlistat-treated patients regained 7%-22% less weight than placebo-treated arms.

#### Adverse Effects

Fatty/oily stool, fecal urgency and oily spotting were the most frequently reported adverse events occurring at rates of 15% to 30% in patients taking orlistat. In 3 studies, approximately 2% (95% CI: 1% to 4%; test for heterogeneity: p=0.09; I<sup>2</sup>=40%) more patients treated with orlistat discontinued treatment due to gastrointestinal side effects compared to placebo. Gastrointestinal side effects were experienced more often by patients treated with orlistat. The percentage experiencing at least 1 gastrointestinal side effect, as

reported in 9 of the 11 trials, was 16% to 40% higher in patients treated with orlistat versus placebo. This difference was statistically significant in all studies. Fecal incontinence was reported as a separate endpoint in 3 studies with an incidence of 6% (95% CI: 5% - 8%; test for heterogeneity:  $p=0.85$ ) higher in orlistat-treated patients.

The conclusion of the Cochrane systematic review was that orlistat was moderately effective in promoting weight loss, but that the studies were limited by attrition and that reported weight loss was from the beginning of the run-in phase rather than the point of randomization. Gastrointestinal side effects were experienced more frequently in patients treated with orlistat. The authors stated that additional studies are needed that are longer in duration and that measure orlistat's effect on cardiovascular morbidity, diabetes, and mortality.

#### **Agency for Healthcare Research and Quality (AHRQ) Evidence Report/Technology Assessment: Pharmacological and Surgical Treatment of Obesity<sup>4</sup>**

The AHRQ performed a meta-analysis including 28 studies. All studies included a dietary intervention in all treatment arms; 39% of studies included educational, behavioral, or psychological interventions; and 18% included exercise as an intervention. The composite patient demographics were as follows: average age 36.7 years, 73% were women, and the average BMI 36.7 kg/m<sup>2</sup>. Further data analysis was stratified by study duration and results are shown below.

**Table 3. Pooled mean weight loss and weight-loss difference for orlistat minus placebo from baseline by study duration**

Study Duration	Number of studies	Mean total weight loss (mean, kg)	Mean weight-loss difference, kg (95% CI)	Test for heterogeneity (p-value)
6 months	11	5.35	2.51 (1.63 – 3.4)	0.00
12 months	21	8.10	2.75 (2.2 – 3.3)	0.00

The frequencies of diarrhea, flatulence, and bloating/abdominal pain/dyspepsia were found to be greater in orlistat-treated patients than placebo, with relative risks of 3.4, 3.1, and 1.5, respectively. The authors calculated that the randomized clinical trials contained a sufficient number of patients to evaluate events occurring at a rate of 2 per 10,000 or greater. The authors point out that adverse events were reported in clinical trials as the frequency of the event rather than the number of patients who experience the event and point out that their analysis may over estimate the number of participants reporting an adverse event.

#### **The National Institute for Clinical Excellence (NICE) Systematic Review<sup>5</sup>**

The NICE systematic review of the clinical effectiveness and cost effectiveness of orlistat was completed in 2001. The methodology was similar to that of other systematic reviews and evaluated 14 clinical trials. Orlistat was shown to reduce a person's weight between 2 to 5 kilograms greater than placebo over a period of a year. This was accompanied by small but significant reductions in total cholesterol and the ratio of total cholesterol to high-density lipids, and in both diastolic and systolic blood pressure. There is no evidence about orlistat's efficacy in reducing a person's weight for periods over 12 months. The resulting clinical guidance stated that in order for patients to be eligible to be treated with orlistat, they must have attempted long-term control of body weight using lifestyle measures without success. They must then embark on a new attempt to lose weight and also have lost 2.5 kg in weight in the month prior to treatment. To continue treatment, a weight loss of at least a further 5% of starting weight after the first three months of orlistat therapy and a cumulative weight loss of at least 10% after the first six months must be documented.

Rissanen et al<sup>7</sup> assessed the clinical usefulness of the NICE published guidelines for the use of orlistat by pooling data from 2 multicenter, randomized, placebo-controlled clinical trials with orlistat. After 2-years, patients who lost at least 5% of their body weight at 12-weeks lost significantly more weight (-11.9%; 95% CI: -13.4 to - 10.3%) than those who lost at least 2.5% during 4-weeks run-in and at least 10% after 6 months (-4.7%; 95% CI: -5.7% to 3.7%),  $p=0.0001$ . In addition, patients who lost 5% or more of their body weight within the initial 12 weeks of treatment had significantly greater improvements in total cholesterol, LDL-cholesterol, triglycerides, fasting glucose, fasting insulin, and systolic and diastolic blood pressures after 2 years compared to those who lost less than 5% of their body weight after 12 weeks. The

authors concluded that weight loss of 5% or greater at 12 weeks accurately predicted sustained improvements in weight and major risk factors, while other suggested criteria are less useful.

#### **XENDOS Study<sup>6</sup>**

This double-blind, placebo-controlled, randomized 3,305 subjects to test the hypothesis that the combination of orlistat 120 mg three times a day and lifestyle changes would lead to greater weight loss and lower the incidence of type 2 diabetes in obese patients over 4 years compared to lifestyle changes and placebo. At the end of 4 years, 52% of subjects in the orlistat group completed the trial compared with 34% taking placebo. Mean weight loss in the orlistat group was 5.8 kg versus 3.0 kg in the placebo group ( $p < 0.0001$ ). The incidence of cumulative new onset diabetes was 6.2% with orlistat and 9.0% with placebo; a risk reduction of 37.3% ( $p = 0.0032$ ). The risk reduction was greatest in persons with an impaired glucose tolerance at baseline. Orlistat's adverse effect profile was similar to that observed in earlier 2 year trials.

#### **Absolute Weight Loss**

At the 12 month point, mean absolute weight loss ranged from -10.6 to -3.29 kg with sibutramine and -6.2 to -1.3 kg for placebo. After 4 years, participants taking orlistat in the XENDOS trial lost an average (LOCF) of 5.8 kg compared to 3.0 kg with placebo.

### **Adverse Events (Safety Data)<sup>2</sup>**

#### **Severe Adverse Events**

Rare cases of hypersensitivity have been reported with the use of orlistat. Signs and symptoms have included pruritus, rash, urticaria, angioedema, bronchospasm and anaphylaxis. Very rare cases of bullous eruption, increase in transaminases and in alkaline phosphatase, and exceptional cases of hepatitis that may be serious have been reported. No causal relationship or physiopathological mechanism between hepatitis and orlistat therapy has been established.

#### **Common Adverse Events**

Gastrointestinal complaints are the most frequently observed adverse events associated with orlistat. The severity of most adverse events experienced was mild and transient and lessened over time.

#### **Other Adverse Events**

**Table 4. Adverse events reported for orlistat and placebo over 1 and 2 years in 7 clinical trials.**

Body System/Adverse Event	Percent of Patients - Year 1		Percent of Patients - Year 2	
	Orlistat N = 1913	Placebo N = 1466	Orlistat N = 613	Placebo N = 524
Digestive				
Oily spotting	26.6	1.3	4.4	0.2
Flatulence with discharge	23.9	1.4	2.1	0.2
Fatty/oily stool	20.0	2.9	5.5	0.6
Oily evacuation	11.9	0.8	2.3	0.2
Increased defecation	10.8	4.1	2.6	0.8
Fecal incontinence	7.7	0.9	1.8	0.2
Rectal pain/discomfort	5.2	4.0	3.3	1.9
Respiratory				
Influenza	39.7	36.2	-	-
Upper respiratory infection	38.1	32.8	26.1	25.8
Lower respiratory infection	7.8	6.6	-	-
Musculoskeletal				
Lower extremity pain	-	-	10.8	10.3
Arthritis	5.4	4.8	-	-
Myalgia	4.2	3.3	-	-
Central Nervous System				
Dizziness	5.2	5.0	-	-

Anxiety	4.7	2.9	2.8	2.1
Depression	-	-	3.4	2.5
Body as a Whole				
Back Pain	13.9	12.1	-	-
Headache	30.6	27.6	-	-
Abdominal pain/discomfort	25.5	21.4	-	-
Fatigue	7.2	6.4	3.1	1.7
Rash	4.3	4.0	-	-
Urogenital				
Menstrual irregularity	9.8	7.5	-	-
Urinary tract infection	7.5	7.5	5.9	4.8

### Tolerability

Early discontinuation due to adverse events occurred in 8.8% of orlistat-treated patients compared to 5% of placebo-treated patients.

### Precautions/Contraindications<sup>2</sup>

#### Precautions

Patients should comply with the advised dietary guidelines as gastrointestinal adverse effects may increase if taken with a diet high in fat (>30% total daily calories from fat). Caution is advised before prescribing orlistat to patients with a history of hyperoxaluria or calcium oxalate nephrolithiasis since some patients may develop increased concentrations of urinary oxalate. Patients with diabetes treated with oral hypoglycemic agents or insulin may experience hypoglycemia following sufficient weight loss to improve metabolic control and require lower doses their diabetes medications. The absorption of some fat-soluble vitamins and beta carotene can be reduced and patients are advised to take a daily multi-vitamin.

#### Contraindications

Orlistat is contraindicated in patients with hypersensitivity to orlistat or any of its components and in patients with chronic malabsorption syndrome or cholestasis.

### Look-alike / Sound-alike (LA / SA) Error Risk Potential

The VA PBM and Center for Medication Safety is conducting a pilot program which queries a multi-attribute drug product search engine for similar sounding and appearing drug names based on orthographic and phonologic similarities, as well as similarities in dosage form, strength and route of administration. Based on similarity scores as well as clinical judgment, the following drug names may be potential sources of drug name confusion:

LA/SA for generic name Orlistat: Orlenta, Uristat

LA/SA for trade name Xenical: Xiral, Xeloda

### Drug Interactions<sup>2</sup>

#### Drug-Drug Interactions

- Cyclosporine's plasma concentrations can be reduced when taken simultaneously with orlistat. Cyclosporine should be taken 2 hours before or after orlistat.
- The absorption of fat soluble vitamins has been shown to be reduced with orlistat. A pharmacokinetic interaction study found that beta-carotene supplement absorption was reduced by 30% when taken simultaneously with orlistat. Orlistat inhibited the absorption of a vitamin E supplement by approximately 60%.
- Vitamin K absorption may be reduced by orlistat. Patients taking warfarin should be monitored closely and their warfarin dose adjusted accordingly.
- Reports of decreased prothrombin, increased INR and unbalanced anticoagulant treatment resulting in change of hemostatic parameters have been reported in patients treated concomitantly with orlistat and anticoagulants.

## **Acquisition Costs**

**Table 5. Cost per day and annual cost for orlistat and sibutramine**

<b>Drug</b>	<b>Dose</b>	<b>Cost/Day/patient (\$)</b>	<b>Cost/Year/patient (\$)</b>
Orlistat capsule	120 mg three times a day	2.40	876.00
Sibutramine capsule	10 mg daily	1.83	667.95
Sibutramine capsule	15 mg daily	2.36	861.40

## **Pharmacoeconomic Analysis**<sup>5,8</sup>

Two economic evaluations have been undertaken for Orlistat and were reported by NICE in 2001: one supplied by orlistat' manufacturer and the other an independent review. The independent review for orlistat estimated a cost per QALY gained of £46,000 (range £19,000 to £55,000). The manufacturer's finding estimated a cost per QALY gained of £10,400 (range £8,400 to £16,000). To attain a sufficient level of cost-effectiveness, in the range of a cost per QALY gained of between £20,000 and £30,000, people treated with orlistat would have to lose about 5% of body mass for each three months that they are maintained on treatment, or achieve a cumulative loss of at least 10% of body weight from the start of treatment over the first six months.

A cost-effectiveness analysis performed by VISN 22 as part of its drug class review in August 2003 estimated the cost of 1 patient to lose 5% or 10% of body weight in a 1 and 2 year period. Costs were based on an average annual cost of orlistat 120 mg three times a day, \$864.32. At 1-year, the number-needed-to-treat (NNT) for 1 patient to lose 5% of their body weight with orlistat was 5 at a cost of \$4321. At 2-years, the NNT was 5 at a total cost of \$8643. The NNT to achieve a 10% weight loss at 1 year with orlistat was 3 and 5 at a cost of \$2593 and \$4321, respectively. At 2-years the NNT was 10 and a total cost of \$17,286.

## **Conclusions**

The use of orlistat in combination with a reduced calorie diet results in modest weight loss after 1 or 2 years. The percentage of patients achieving a 5% or 10% loss of body weight was greater with orlistat. The longest clinical trial experience with orlistat is 4 years. Orlistat has also demonstrated statistically significant improvements in metabolic parameters such as lipids and glycemic control, and blood pressure. Orlistat in one trial was shown to reduce the incidence of type 2 diabetes in obese patients. The significance of these changes, including orlistat-attributed weight loss, on clinical outcomes such as mortality, cardiovascular events, stroke, and reduced medication burden for chronic illnesses is unknown.

Gastrointestinal complaints including oily stools, fecal urgency and incontinence commonly reported adverse events that can compromise adherence to therapy. Patients can minimize this by limiting the amount of fat in their diet.

Middle-aged, caucasian, women accounted for a large majority of participants in orlistat clinical trials and do not accurately represent the current VA population. As such extrapolation of the clinical trial data should be done cautiously.

## **Formulary Decision**

- Orlistat will remain non-formulary at VANF and VISN level, patients currently prescribed orlistat be grandfathered.
- Patients must meet criteria-for-use and a nonformulary request must be completed.

## **References:**

1. The Department of Veterans Affairs National Center for Health Promotion and Disease Prevention developed the Managing Overweight/Obesity for Veterans Everywhere (MOVE) program <http://vaww.nchdpd.med.va.gov/MOVEIntro.asp>, accessed November 2004.
2. Xenical (Orlistat) Package Insert, Roche Laboratories, Nutley, NJ, September 2000. Revised label from September 2, 2005 accessed September 8, 2005.
3. Padwal R, Li SK, Lau DCW. Long-term pharmacotherapy for obesity and overweight. The Cochrane Database of Systematic Reviews 2004, volume 3.

4. Shekelle PG, Morton SC, Maglione MA, Suttrop M, Tu W, Li Z, Maggard M, Mojica WA, Shugarman L, Solomon V, Jungvig L, Newberry SJ, Mead D, Rhodes S. Pharmacological and Surgical Treatment of Obesity. Evidence Report/Technology Assessment No. 103. (Prepared by the Southern California–RAND Evidence-Based Practice Center, Santa Monica, CA, under contract Number 290-02-0003.) AHRQ Publication No. 04-E028-2. Rockville, MD: Agency for Healthcare Research and Quality. July 2004.
5. National Institute for Clinical Excellence. Orlistat for the treatment of obesity in adults, 2001, Accessed at <http://www.nice.org.uk/pdf/orlistatguidance.pdf>, December 2004.
6. Torgerson JS, Boldrin MN, Hauptman J, et al. XENical in the prevention of diabetes in obese subjects (XENDOS) study. *Diabetes Care* 2004;27:155-61.
7. Rissanen A, Lean M, Rossner S, et al. Predictive value of early weight loss in obesity management with orlistat: an evidence-based assessment of prescribing guidelines. *International Journal of Obesity* 2003;27:103-9.
8. VISN 22 Drug Class Review: Antiobesity Medications. August 2003.

---

Originally prepared January 2005. Contact person: Todd Semla, MS, Pharm.D., BCPS

---